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STABILITY OF PHARMACEUTICAL PREPARATIONS

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Abstract

Pharmaceutical product must be chemically, physically and therapeutically stable to ensure the health and preventive aspect. We have to study the effect of many factors on drug formulation as well as packaging and storage. Stability of pharmaceutical preparation act as the identity card of the drug to reach the pharmacy, the hospital, and the consumer in general, without this identity, it is not possible to approve the drug healthily or in circulation. Furthermore, stability mentoring of pharmaceutical preparations provides information about many physiochemical parameters as rate, and order of decomposition reaction of active ingredients, or the expected interaction with the other ingredients. In order to follow the stability of any pharmaceutical product, an analytical method must be available and convenient for the chemical nature of the product, the analytical procedure must be validated by the accuracy, precision, recovery as well as sensitivity, selectivity proved with statistical calculations such as t-test, and f-test.

Keywords: Stability, Pharmaceutical Preparations, Accelerated Conditions.

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Introduction

- Factors affect the stability of pharmaceutical preparations

The stability of the pharmaceutical preparations refers to chemical, physical, microbiological, therapeutic and toxic properties of active component in the pharmaceuticals within certain limits and with the same standard levels of preparation until it reaches the patient as well as in the hands of the patient (1), the stability may be affecting by many factors including:

1-Chemicals like the presence of oxidant

2-Light which may cause in photo degradations

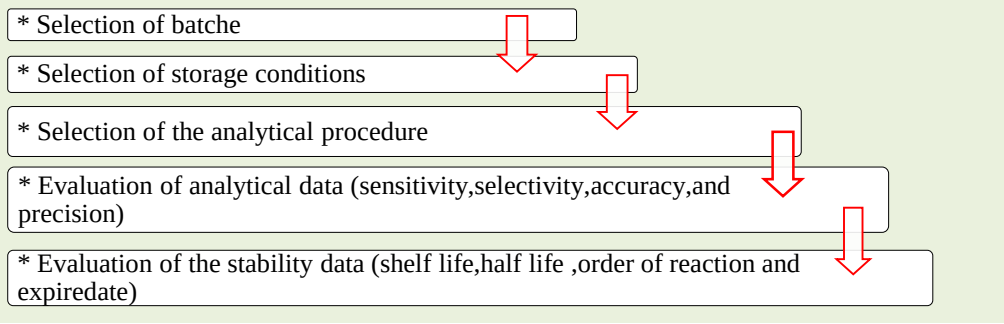
3- Temperature may induce a specific decomposition or reaction

4- Moister which may cause in hydrolysis reaction, cleavage of amide, or ester (2).

Pharmaceutical products must be stable during packing, storage, transformation, and distribution; therefore, the container and closure system have an impact on the stability period (3) for example the improper packaging and storage conditions reduce the quality of amoxicillin–clavulanic acid preparations (4). Strict quality control measures are urgently needed to maintain the quality of amoxicillin–clavulanic acid in tropical countries. The design of the stability studies are based on the type of active component, functional groups and properties but it can be evaluated by follow the amount of the active ingredient and the rates of its decomposition, degradation or dissociation under different conditions over time (2),for example paracetamol exhibits about 20% degradation when it exposed to base, and oxidizing agent, in comparative with other forced conditions moisture, acid and reducing agents (5), which can be calculated or predicted by accelerated storage conditions to know the rate of decomposition at different temperatures or may be ultrahigh temperatures then apply Arrhenius equation to obtain the rate constants at 25 degrees Celsius (6).The classical approach of Arrhenius uses the linear regression equation between drug content against time followed by relationship of reciprocal temperature with logarithm of content of the active component to predict the rate constant at room temperature as well as the shelf-life of the drug (7).

- Accelerating conditions

Accelerating conditions for studying stability is useful in prediction the pathway of degradation, evaluating the kinetic data (rate of degradation, rate constant, and activation energy), and for evaluation the analytical data. It may follow the steps in the scheme below (8):


* Selection of batche
* Selection of storage conditions
* Selection of the analytical procedure
* Evaluation of analytical data (sensitivity,selectivity,accuracy,and precision)
* Evaluation of the stability data (shelf life,half life ,order of reaction and expiredate)

Scheme 1. The main steps of stability study

Accelerating storage conditions involve mainly storage under higher or lower temperature than room or ordinary room temperature for example accelerating 14 days storage period of cefazolin ophthalmic solution exhibit that 4◦C is the best storage temperature for this preparation (9). Drugs may degradative by either reversible or

irreversible processes. It is always obeyed first order reaction in which the active ingredient decomposes, while it is seldom occur or consider second order in which it reacts with another ingredient (10).

- **Shelf life**

Shelf life is an index of safety and efficacy for the acceptance and approval of any pharmaceutical product (11), it also indicates the quality of the product and the efficiency of the manufacturer (12). Shelf life is estimated by real-time procedure as well as accelerated conditions, low estimated shelf life of manufactured drug may lead to evaluating new formulations with particular attention to experimental design (13). The shelf life of metronidazole liquid formulation increases by increases its stability about 3.7-5.9 times in 20%-100%v/v propylene glycol more than aqueous solution (14). The stability of suspensions formulation of levofloxacin was also enhanced with more than 96% in three selected vehicles (15), while amoxicillin clavulanate exhibits low shelf life because it decomposes to be 80% after the fifth day of preparation and 70% after another two days when it prepared as suspensions and storage at 5-29°C over a period of 10 days (16).

-Formulation processing and testing methods

Stability study must be followed for the dosage formulation processing and testing methods not for standard active martials because each dosage form requires different processing during preparations as lyophilization, spray drying, aqueous film coating, wet granulation or recrystallization, these processing may cause in physical and chemical change of the active ingredient, such as dissolution rate, decomposition rate, flow rate and compatibility (17).Stability testing of pharmaceuticals includes rather than assay of active ingredient, other important testing such as appearance (color, odor, and texture), Identification (uv, I.R, NMR spectrum, and chromatogram), Purities and dissolution (17). More complicated techniques may be required to improve the stability of dosage forms such as crystallographic (18)

Cefuroxime sodium (50 mg/ml) is prepared as injection in 0.9% sodium chloride solution and stored in polypropylene syringes, its stability was studied at 25 and 5 °C by high-performance liquid chromatographic method in which the concentration of the drug was directly related to peak heights with percent relative standard deviation RSD% of five replications was 0.9 (19).

The presence of different additives in liquid dosage forms as preservative, and antioxidants are also affecting on stability including types and levels (20), biopharmaceutical products in storage change as they age, and must be stable within the shelf life (21).

The light increases the degradations of some dosage forms; therefore, the addition of some stabilizer is necessary, many light sources has been used to study the photostability of tetracycline hydrochloride solutions in the presence of different stabilizers. Glutathione as a stabilizer was found to be less affected (22)

Conclusion

Stability of pharmaceutical preparation act as the identity card of the drugs, it can be followed by accelerating storage conditions of the selected batch, the stability testing may require qualitative and quantitative analysis, the higher stable dosage forms are the longer shelf life, stability studies also provide information about the behavior of the active ingredient in drugs formulation against wide variety of variables.

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